

### REMARKS

The Office Action, dated September 19, 2008, has been reviewed and the Examiner's comments carefully considered. The present Amendment modifies claims 1, 8, 18, 20, 30, 36-39, 41, 43, 44, 46, 53-55, 65-67, and 69, all in accordance with the originally-filed specification. No new matter has been added. Accordingly, claims 1-5, 7-9, 11, 18-20, 22, 23, 25, 30-32, 36-39, 41, 43, 44, 46, 53-55, 65-67, and 69 are pending in this application, and claims 1, 36 and 69 are in independent form.

In the Office Action, the pending claims stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,416,959 to Giuliano et al. (hereinafter "the Giuliano patent"). In view of the foregoing amendments and the following remarks, Applicants respectfully request reconsideration of these rejections.

#### Summary of the Claimed Embodiments

Independent claim 1, as amended, provides a tissue engineered construct analytical imaging system for use in connection with at least one culture well having a tissue engineered construct therein and positionable in an enclosed environment. The system includes an imaging device positioned within the enclosed environment for obtaining three-dimensional image data reflective of at least a portion of the tissue engineered construct in a well area of interest in the at least one culture well, without the removal of the culture well from the enclosed environment. The system further includes a computer controller for: receiving data from the imaging device; analyzing the data for determining at least one desired parameter within the well area of interest; and/or outputting data reflecting results of an analysis.

As set forth in independent claim 36, as amended, provided is a computer-implemented method of obtaining and analyzing images of a tissue engineered construct. This method includes: (a) positioning at least one culture well having the tissue engineered

construct therein in an enclosed environment; and (b) obtaining, from an imaging device positioned within the enclosed environment, three-dimensional image data reflective of at least a portion of the tissue engineered construct in a well area of interest in the at least one culture well, without the removal of the culture well from the enclosed environment.

Finally, independent claim 69 of the present application, as amended, is directed to a tissue engineered construct imaging and analysis apparatus for use in connection with at least one culture well having tissue engineered constructs therein and positionable in an enclosed environment. The apparatus includes imaging means positionable in the enclosed environment and for obtaining three-dimensional image data reflective of at least a portion of the tissue engineered construct in a well area of interest in the at least one culture well, without the removal of the culture well from the enclosed environment.

#### The Cited Prior Art

The sole reference cited by the Examiner in the Office Action, the Giuliano patent, is directed to a system for cell-based screening, with specific and particular focus on analyzing two-dimensional cellular systems. In particular, and according to the methods and systems in the Giuliano patent, a group of cells (or a colony) is grown from single cells, and certain parameters are measured for this cellular material in a two-dimensional format. For example, the cells may be optically screened and analyzed to determine distribution, environment, activity relating to particular biological functions. In particular, it appears that the system of the Giuliano patent is for specific use in drug screening based upon cell activity.

With respect to the device and arrangement of the Giuliano patent, an inverted fluorescence microscope 1 is used to obtain images of materials in a plate 4, which is movable using an XY stage 3, in particular, a joystick 6. This joystick 6 allows for the

manual movement of the stage in various directions. A high resolution digital camera 7 acquires images from each well or location on the plate, and an automated controller 9 and central processing unit 10 allow for the various control aspects of the system. Accordingly, the system of the Giuliano patent is a microscope-based data collection and processing system.

The Cited Prior Art Does Not Teach or Suggest  
the System of Claim 1, Method of Claim 36, or Apparatus of Claim 69

As discussed above, the primary reference, i.e., the Giuliano patent, represents a well-known data collection system for use in connection with a known microscope device. For example, at column 10, lines 60-61, the Giuliano patent specifically recites that the microscope 1 may be a Zeiss Axiovert inverted fluorescence microscope which uses standard objectives with magnification of 1-100x to the camera. Further, and as discussed above, the Giuliano patent is a system for cell-based screening for use in connection with two-dimensional cellular systems where a group of cells is grown from an individual cell. Thereafter, the system is used for drug screening and similar analytical processes.

With respect to the present invention, it is specifically designed and arranged for use in connection with tissue engineered constructs, such as bioartificial tissue cellular constructs, bioartificial tendons, etc. In that regard, the image data obtained by the imaging device in the presently-invented system acquires three-dimensional image data in order to measure and determine various parameters, e.g., matrix compaction, organization, contraction, and other similar parameters that are normally performed manually by periodically removing the culture plates from the controlled environment.

Next, and according to the prior art, in order to make such measurements and acquire this important information and data, the tissue engineered constructs (i.e., the construct in the culture well) must be removed from the controlled environment in order to

access an external imaging device, such as a camera or scanner. Depending upon the effect of being measured, this process may either be repeated every few hours, days, etc., which represents a labor-intensive process and may lead to the damage of the constructs themselves. The present invention allows for the appropriate imaging of these tissue engineered constructs which occurs while the tissue engineered construct remains positioned within the enclosed environment, which is achieved by arranging the system where the imaging device is within the enclosed environment. Such a novel and inventive arrangement allows for the capture of appropriate three-dimensional tissue engineered construct image data from the material within the enclosed environment, and transfer this data to an outside computer controller or other system.

Again, the system of the Giuliano patent provides an inverted fluorescence microscope 1 having a movable XY stage 3 for moving the plate 4 in the X-direction and Y-direction, as well as a drive 5 for moving the objective in the Z-direction (for focusing). A high resolution digital camera 7 acquires images from each well. Therefore, it is clear that the Giuliano system is different than the presently-invented system, method and apparatus in at least two areas, namely: (1) the present invention captures three-dimensional image data related to a tissue engineered construct; and (2) the imaging device is positioned within the enclosed environment in order to ensure the efficient and effective collection of this three-dimensional image data, without the need for removing the culture well from this enclosed environment. The Giuliano system neither teaches nor suggests either of these features. In particular, while the Giuliano system discusses an imaging device, as plainly illustrated in Figs. 1 and 2 of the Giuliano patent, the imaging device is not positioned within an enclosed environment. Further, the system of the Giuliano patent is directed to the collection of two-dimensional image data in connection with specific cellular material, as opposed to the three-dimensional image data of a tissue engineered construct (as described and claimed in the

present application).

Therefore, it is submitted that neither the Giuliano nor any of the prior art of record, whether used alone or in combination, teaches or suggests the tissue engineered construct analytical imaging system of independent claim 1, which recites "an imaging device positioned within the enclosed environment and configured to obtain three-dimensional image data reflective of at least a portion of the tissue engineered construct in a well area of interest and the at least one culture cell, without the removal of the culture well from the enclosed environment," the computer-implemented method of claim 36, which recites "obtaining, from an imaging device positioned within the enclosed environment, three-dimensional image data reflective of at least a portion of the tissue engineered construct in a well area of interest in the at least one culture well, without the removal of the culture well from the enclosed environment," and the apparatus of independent claim 69, which recites "imaging means positionable in the enclosed environment and for obtaining three-dimensional image data reflective of at least a portion of the tissue engineered construct in a well area of interest in the at least one culture well, without the removal of the culture well from the enclosed environment."

#### Summary

For the foregoing reasons, independent claims 1, 36, and 69, as amended, are not anticipated by or rendered obvious over the Giuliano patent or any of the prior art of record, whether used alone or in combination. Reconsideration of the rejection of independent claims 1, 36, and 69 is respectfully requested. Claims 2-5, 7-9, 11, 18-20, 22, 23, 25, and 30-32 depend either directly or indirectly from and add further limitations to independent claims 1 and are believed to be allowable for at least the reasons discussed hereinabove in connection with independent claims 1. Therefore, for all the above reasons,

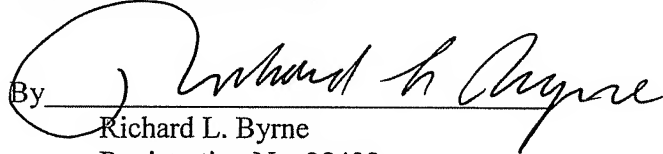
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reconsideration of the rejections of claims 2-5, 7-9, 11, 18-20, 22, 23, 25, and 30-32 is respectfully requested. Claims 37-39, 41, 43, 44, 46, 53-55, and 65-67 depend either directly or indirectly from and add further limitations to independent claim 36 and are believed to be allowable for at least the reasons discussed hereinabove in connection with independent claim 36. Therefore, for all the above reasons, reconsideration of the rejections of claims 37-39, 41, 43, 44, 46, 53-55, and 65-67 is respectfully requested.

For all the foregoing reasons, Applicants believe that claims 1-5, 7-9, 11, 18-20, 22, 23, 25, 30-32, 36-39, 41, 43, 44, 46, 53-55, 65-67, and 69, as amended, are patentable over the cited prior art and in condition for allowance. Reconsideration and allowance of all pending claims 1-5, 7-9, 11, 18-20, 22, 23, 25, 30-32, 36-39, 41, 43, 44, 46, 53-55, 65-67, and 69 are respectfully requested.

Respectfully submitted,

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